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Carboplatin Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Is Safe and Efficacious in Recurrent and Advanced Ovarian Cancer

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Mentor: Jason Foster

Program: General Surgery

Type: Original Research

Background: HIPEC with cisplatin in recurrent and advanced ovarian cancer (AOC) improves survival, but renal toxicity is common, even with renal protectants. Carboplatin intravenous (IV) and intraperitoneal (IP) have significantly less nephrotoxicity with comparable efficacy. This study reports the safety and efficacy of carboplatin HIPEC for recurrent and AOC.

Methods: Retrospective analysis of a cytoreductive surgery (CRS) /HIPEC registry was performed on recurrent and AOC patients treated between 2012-2018 with and without HIPEC. HIPEC with carboplatin (600-800 mg/mM2) was delivered for 90 minutes at 41-42 C. Peritoneal Cancer Index (PCI), Completeness of Cytoreduction (CC)-score, nephrotoxicity by RIFLE score, thrombocytopenia, pancytopenia, length of stay (LOS), progression free survival (PFS), overall survival (OS), peritoneal relapse and all relapse events were collected and compared from the date of surgery.

Results: A total of 34 recurrent and AOC patients had CRS, 21 treated with HIPEC. Mean PCI for CRS and CRS/HIPEC was 23 and 22 respectively. 95% HIPEC and 100% no HIPEC had R0/R1/R2a. 9% developed >grade 1 AKI. Thrombocytopenia (platelet < 75K) occurred in 23% of HIPEC patients. LOS was 9.5 days for both groups. Post-CRS OS was 15 vs. 56 months for CRS vs. CRS/HIPEC, p<0.01. There was no difference in median OS in HIPEC group treated at recurrence or first CRS. Peritoneal recurrence was 69% for CRS vs 19% for CRS/HIPEC, p<0.01.

Conclusion: This data demonstrates that Carboplatin HIPEC has similar efficacy to cisplatin without the nephrotoxicity. Carboplatin HIPEC for recurrent and AOC is safe and efficacious. The survival benefit may be attributable to peritoneal disease control and peritoneal relapse free survival may be a viable endpoint in future HIPEC clinical trials. ■

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Table 1.

Hyperthermic Intraperitoneal Chemotherapy (HIPEC) group demonstrates increased overall survival (OS), reduced rate of peritoneal relapse, and similar overall relapse rate when compared with non-HIPEC group. Upfront HIPEC is associated with lower peritoneal relapse rate when compared with HIPEC performed after disease recurrence.

GROUP	#	OSCRS months	DOD (n=34)	NED (n=34)	PERITONEAL RELAPSE	ANY RELAPSE
ALL	34	**34**	-	-	**-**	-
No HIPEC	13	**20**	73%	0%	**69%**	87%
HIPEC	21	**56**	42%	38%	**19%**	79%
$HIPEC_{recurrent}$	9	**56**	33%	15%	**33%**	92%
$HIPEC_{upfront}$	12	**56**	23%	58%	**8%**	67%

Exploring Head and Neck (H&N) Melanoma Sentinel Lymph Node (SLN) Outcome Compliance With Multicenter Selective Lymphadenectomy Trials (MSLT) Predicted Outcome

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Program: General Surgery

Type: Original Research

Background: MSLT established SLN management in extremity/trunk melanoma, demonstrating a 16% positive SLN (+SLN) rate and 14% positive non-SLN rate (+NSLN) in Complete Lymph Node Dissection (CLND). CLND improved Disease Specific Survival (DSS) without Overall Survival (OS) benefit. Results of MSLT guide H&N melanoma but H&N only represented 13% of patients in MSLT II. This project explored the validity of observations reported in MSLT II in H&N melanoma.

Methods: Retrospective H&N melanoma population treated 2005-2019. 124 ≥T1b with SLN injection and 108 SLN dissections were performed. Complication rates, T-stage, rates of +SLN, +NSLN in CLND were calculated, as well as death due to disease (DOD), progression free survival (PFS), along with rates of local (LR), nodal (LNR), and systemic (SR) recurrence.

Results: T-stage was 41% IB, 23% IIA, 28% IIB, 8% IIC. Nerve complication was 4% for SLN and 11% for CLND. – SLN group survival is 93% compare to survival of 70% for +SLN group with median follow-up of 40 months. Rate of +SLN was 29% and +NSLN rate for CLND was 50%. Patients with positive SLN but did not undergo CLND (+SLNBx only) has surprisingly lower rate of LR, LNR, SR, and DOD when compared to patients with positive SLN who underwent CLND (CLND group). (Table 1.)

Conclusion: +SLN rate was 2-fold higher and +NSLN following CLND was 3-fold higher in H&N melanoma. Local regional recurrence rates were higher for CLND compared to SLNB+ only. These results support nodal

behavior and failure patterns in H&N may be different from trunk/extremity, supporting consideration of dedicated H&N trial. ■

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Table 1.
+SLN group demonstrates higher rate of local (LR), nodal (LNR), and systemic (SR) recurrence, as well as higher rate of death due to disease (DOD) when compared with -SLN group. Within +SLN group, patients who underwent complete lymph node dissection (CLND) surprisingly have higher rate of LR, LNR, SR, and DOD.

Completed SLNBx (N= 108)	LR %	LNR %	Local/Regional recurrence %	SR %	Combined Sys/Nodal %	DOD %	NED %
SLN –ve (77)	18%	8%	21%	13%	1%	7%	93%
SLN +ve (31)	23%	32%	35%	45%	29%	29%	55%
CLND (20)	**35%**	**45%**	**55%**	55%	40%	35%	45%
+SLNBx only (11)	**0%**	**9%**	**9%**	27%	9%	18%	73%
p-value	**0.03***	**0.055**	**0.02***	0.26	0.15	0.43	0.26

Thiamine Supplementation Does Not Improve Outcomes in Hospitalized Patients With Encephalopathy

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Program: Neurology

Type: Original Research

Background: In hospitalized and critically ill patients, thiamine deficiency is common, difficult to clinically diagnose, and increases risk for encephalopathy.1,2 Thiamine supplementation for patients with encephalopathy has become routine at UNMC for its safety and potential benefits. We hypothesized that thiamine supplementation in hospitalized patients with encephalopathy would decrease their length of stay (LOS).

Methods: Adults (age >19 years) with index admission to UNMC between 1/1/2017 and 12/31/2017, hospital stay of 3-30 days, and ICD-10 code associated with encephalopathy were identified by the hospital electronic health record data access core. Primary outcome was hospital LOS, which we log-transformed due to skewness. Model adjusted mean log LOS estimates were exponentiated to obtain geometric means. Patients in the Thiamine group received at least one dose of supplemental thiamine (including multivitamins). A general linear model was used to evaluate the association between log LOS and thiamine supplementation.

Results: We identified 985 patients who met the above criteria. Table 1 describes the cohort demographics and clinical characteristics. After adjusting for potential confounding variables (denoted in Table 1), the mean log LOS was 1.95 for the Thiamine group and 1.63 for the No Thiamine group (p <0.0001).

Table 1.
Demographic and clinical characteristics of hospitalized patients with encephalopathy.

	No. (%), unless specified		
	Thiamine Group (n = 178)	No Thiamine Group (n = 807)	P-value
Demographic Information			
Age (mean ± SD)*	66.5 ± 18.1	59.4 ± 15.5	<0.0001a
Gender*			0.0004
Female	67 (37.6)	423 (52.4)	
Male	111 (62.4)	384 (47.6)	
Race			0.47
Black	32 (18.4)	119 (14.8)	
White	129 (74.1)	627 (78.1)	
Other	13 (7.5)	57 (7.1)	
Ethnicity			0.65
Hispanic	8 (4.5)	43 (5.3)	
Not Hispanic	170 (95.5)	763 (94.7)	
Work status			<0.0001
Disabled	44 (25.1)	166 (20.7)	
Employed/Student/Retired	81 (46.3)	524 (65.3)	
Not employed	50 (28.6)	112 (14.0)	
Insurance status*			0.004
Insured	151 (84.8)	741 (91.8)	
Not insured	27 (15.2)	66 (8.2)	
Clinical Characteristics			
Log (DRG weight) (mean ± SD)	0.43 ± 0.64	0.26 ± 0.53	0.001a
Alcohol use*	68 (51.9)	166 (26.0)	<0.0001
PMH of malabsorption	20 (11.2)	115 (14.3)	0.29
PMH of GI disease	22 (12.4)	113 (14.0)	0.56
PMH of malnutrition*	46 (25.8)	167 (20.7)	0.13
PMH of cancer	40 (22.5)	220 (27.3)	0.19
PMH of GI surgery	28 (15.7)	98 (12.1)	0.19
Home use of loop diuretics	4 (2.2)	17 (2.1)	0.78b
Home use of PPIs	1 (0.6)	17 (2.1)	0.22b
Sepsis during hospital stay*	46 (25.8)	193 (23.9)	0.59
DKA during hospital stay*	27 (15.2)	72 (8.9)	0.01
Neurology service consulted*	57 (32.0)	141 (17.5)	<0.0001
Outcomes			
Log (Length of stay) (mean ± SD)	1.98 ± 0.70	1.60 ± 0.60	<0.0001a

Abbreviations: SD = standard deviation. DRG = diagnosis-related group. PMH = past medical history. GI = gastrointestinal. DKA = diabetic ketoacidosis. LOS = length of stay.

P-values from Chi-Square tests, unless otherwise specified.
a P-values from t-test.
b P-values from Fisher's exact test.
* Potential confounding variables that can contribute to log (LOS) via linear model.

Demographic information, clinical characteristics, and primary outcome were compared between the Thiamine group and No Thiamine group.